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An evaluation of risk factors for overall complications after curative gastrectomy in gastric cancer patients aged 65 or over

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ABSTRACT

Aims: The purpose of this study was to identify risk factors for postoperative complications in patients with gastric cancer aged 65 or over.

Methods: Data from medical records in our database were reviewed and analyzed retrospectively. Two hundred twenty-nine patients with histologically confirmed gastric cancer underwent curative gastrectomy in our clinic between January 2017 and December 2021. Eighty-eight patients younger than 65 and 21 with previous histories of abdominal surgery, multi-visceral resection, emergency surgery due to perforation, bleeding, or obstruction, 18 with preoperative radiotherapy or chemotherapy were excluded. The remaining 102 patients, aged 65 years or over, were included in the study. Patient characteristics, intraoperative findings, and postoperative complications were evaluated.

Results: Postoperative complications with Clavien–Dindo grade ≥ II were observed in 29 patients (28.4%). Univariate analysis showed that the prognostic nutritional index (<45) (odds ratio 0.91; 95% confidence interval, 0.86-0.97; p = 0.004), controlling nutritional status score (≥5) (odds ratio 1.27; 95% confidence interval, 1.09-1.49; p = 0.002), and body mass index (BMI) (≥25 kg/m²) (odds ratio 1.97; 95% confidence interval, 1.00-1.26; p = 0.042) significantly predicted postoperative complications. Multivariate analysis showed that BMI (≥25 kg/m²) (odds ratio 1.18; 95% confidence interval, 1.03-1.34; p = 0.011) significantly predicted postoperative complications.

Conclusion: The overall postoperative complication risk among older individuals with gastric cancer who underwent curative gastrectomy was significantly higher among high-BMI patients. Perioperative management with a focus on BMI is important in older patients undergoing elective curative gastrectomy.

Keywords: Gastric cancer, older patients, postoperative complication, risk factor

INTRODUCTION

The number of individuals aged 65 years or older in Turkey has increased rapidly in recent years. In 2016, older individuals accounted for 8.3% of the Turkish population. Five years later, by 2021, this had increased by 24.0% to 9.7% of the population. Projections predicted that the elderly would represent 11.0% of the population by 2025.1 This increase reflects the aging of Turkish society. Due to the aging population, the numbers and mean ages of patients diagnosed with various cancers, including gastric cancer, have also risen.2 Older patients have a higher incidence of postoperative complications caused by decreased physiological function. Additionally, rates of underlying diseases are higher in this age group, meaning that complications tend to be more severe.2-4 Although some studies have described age as a significant predictive factor for postoperative morbidity after gastric cancer surgery, no significant predictive factor postoperative complications among older individuals has yet been identified.5-7 Due to the increasing rates of gastrectomy procedures among older gastric cancer patients, clinical factors capable of predicting postoperative complications are of significant interest in terms of making adjustments to the surgical strategy. This single-center, retrospective study is planned from that perspective. In the light of the previous literature, potential predictive factors were prioritized based on their simplicity, objectivity, and preoperative availability. Analysis was then performed to identify whether any of these factors were significantly correlated with overall complications after curative gastrectomy in patients aged 65 years or older.

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METHODS

The study was carried out with the permission of Samsun University Medical Faculty Clinical Researches Ethics Committee (Date: 21.10.2021, Decision No: GOKA/2021/21/10). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study retrospectively reviewed and analyzed data from medical records stored in our database. Two hundred twenty-nine patients with histologically confirmed gastric cancer underwent curative gastrectomy in our clinic between January 2017 and December 2021. Eighty-eight patients younger than 65, and 21 with previous histories of gastric surgery, multi-visceral resection, emergency surgery due to perforation, bleeding, or obstruction, 18 with preoperative radiotherapy or chemotherapy were excluded. The remaining 102 patients aged 65 or over were included in the study.

The preoperative index involved age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) grade, comorbidities (diabetes mellitus, hypertension, chronic obstructive pulmonary disease, cerebral infarction, and ischemic heart disease) and laboratory data obtained from baseline investigation performed within one month prior to surgery (neutrophil count, lymphocyte count, serum albumin, and total cholesterol). Perioperative data were noted, including the extent of resection, combined resection, operative time, and surgical procedure. Postoperative characteristics included tumor depth, nodal satus, and short-term complications. Postoperative short-term complications were defined as morbidity and mortality occurring during hospitalization or within 30 days after surgery. The complications were classified using the Clavien-Dindo (CD) system.8 Patient staging was adjusted according to the 8th edition of the American Joint Cancer Committee staging system after pathological examination.9

Nutrition is a well defined risk factor for postoperative morbidity and mortality.10,11 Nutrition assessment tools incorporating inflammatory factors, such as the prognostic nutritional index (PNI) and controlling nutritional status (CONUT) score, and the neutrophil to lymphocyte ratio (NLR) as an inflammatory marker, have been developed to predict postoperative morbidity and mortality in various cancers after radical surgeries.12-15 NLR was calculated by dividing the neutrophil count by the lymphocyte count. NLR <2.5 was defined as low and NLR ≥ 2.5 as high.16 PNI was calculated using the equation (10 x serum albumin (g/ dL) + (0.005 x total lymphocyte count). PNI scores <45 were defined as low and scores ≥ 45 as high.17 The CONUT score was calculated using the method shown in **Table 1**. CONUT scores <5 were defined as low and scores ≥ 5 as high.18 One of the simplest indicators of physical constitution, body mass index (BMI) was calculated as body weight (kilograms) divided by height (meters) squared. Values higher than 18.5 kg/m² and lower than 25.0 kg/m² were regarded as normal BMI, and values below 18.5 kg/m² as low BMI.

Statistical Analysis

Univariate and multivariate logistic regression models were used to determine the factors associated with postoperative complications following gastrectomy. Variables with p values <0.05 identified at univariate analysis were fitted into the multivariate model and analyzed after adjusting for potential confounders using the forced-entry method. Statistical significance was set at p <0.05. All statistical analyses were performed on Statistical Package for the Social Sciences (SPSS) software (SPSS Inc., Chicago, IL, USA).

RESULTS

The median age of the study population was 72 years (range, 65 – 92), and 72.5% were male. More than 90% of patients exhibited ASA prognostic stage ≥2, and 86.2% had at least one comorbidity such as diabetes mellitus or hypertension that required treatment with medication. The median BMI was 25 kg/m² (range, 16-35). Sixty percent of the study population had BMIs exceeding 25 kg/m². The median PNI, CONUT scores and NLR were 41.2 (range, 15-60.5), 3 (range, 0-12), 4 (range, 1.2-22.6), respectively. In terms of surgical outcomes, distal and total gastrectomies were performed on 28.5% and 71.5% of patients, respectively, and laparoscopic surgery on 26.5%. The median operative time and intraoperative bleeding were 175 minute (range, 100-360 minute), 60 ml (range, 20-300 ml), respectively. Clavien-Dindo complications ≥Grade II complications were observed in 29 (28.4%) patients; Grade II in 18 (17.64%) patients, Grade IV in 3 (2.94%), Grade V in 8 (7.84%). Ileus occurred in two patients (1.96%), surgical site infection in eight (7.84%), atelectasis in six (5.88%), pneumonia in five (4.9%), acute myocardial infarction in five (4.9%), acute cerebrovascular event in two (1.86%), and pulmonary embolism in one (0.98%). Pathological stage I, II, III accounted for 9.8%, 16.6%, and 73.6% of patients, respectively. In terms of the correlation between clinical factors and the overall complications (**Table 2**), univariate analysis identified BMI (p=0.039), PNI (p=0.004), CONUT score (p=0.002) as significantly correlated with the occurrence of overall complications. Multivariate analysis including these factors revealed that BMI 25 kg/m² or higher was the only factor significantly correlated with the occurrence of overall complications (p=0.011).

Table 1. Scoring system for the controlling nutritional status (CONUT)

Degree of undernutrition	CONUT score	Serum albumin (g/dl)	Total lymphocyte(/mm3)	Total cholesterol (mg/dl)
Normal	0-1	≥3.50 (0)	≥1,600 (0)	≥180 (0)
Mild	2-4	3.00-3.49 (2)	1,200-1,599 (1)	140-179 (1)
Moderate	5-8	2.50-2.99 (4)	8.00-1,199 (2)	100-139 (2)
Severe	9-12	<2.5 (6)	<800 (3)	<100 (3)

CONUT score =Serum albumin score + total lymphocyte score + total cholesterol score

Table 2. Univariate and multivariate analyses to identify risk factors for the occurrence of overall complication

	Univariate analysis OR (95% CI)	p value	Multivariate analysis OR (95% CI)	p value
Sex (Female)	0.99 (0.37-2.59)	0.985		
Age	1.04 (0.98-1.11)	0.183		
BMI≥25 kg/m²	1.12 (1.00-1.26)	0.039	1.18 (1.03-1.34)	0.011
ASA-PS (≥2)	0.56 (0.09-3.65)	0.561		
DM	2.36 (0.92-6.05)	0.073		
HT	1.44 (0.54-3.86)	0.463		
IHD	2.14 (0.89-5.15)	0.087		
COPD	1.27 (0.22-7.38)	0.784		
CI	2.57 (0.15-42.53)	0.509		
NLR≥2.5	1.08 (0.99-1.19)	0.071		
PNI<45	0.91 (0.86-0.97)	0.004	0.96(0.84-1.09)	0.590
CONUT≥5	1.27 (1.09-1.49)	0.002	1.22(0.85-1.74)	0.264
Bleeding	0.99 (0.98-1.00)	0.095		
Operative time	1.00 (0.99-1.01)	0.371		
Surgical procedure	0.83 (0.32-2.14)	0.714		
Surgical approach	0.64 (0.23-1.81)	0.406		
Stage 2-3	1.66 (0.33-8.33)	0.537		

CI: confidence interval; OR: odds ratio; ASA-PS: American Society of Anesthesiologists Physical Status; BMI: body mass index; DM: diabetes mellitus; HT: hypertension; IHD: ischemic heart disease; COPD: chronic obstructive pulmonary disease; CI: cerebral infarction; PNI: prognostic nutritional index; CONUT: controlling nutritional status score, NLR: neutrophil to lymphocyte ratio

DISCUSSION

Life expectancy and average age are both steadily rising in Turkey. The increase in the average age is also accompanied by a higher prevalence of various types of cancers, one of those affecting the older population being gastric cancer. As the rate of gastrectomy procedures in older patients is rising, clinical factors capable of predicting postoperative complications are of particular interest in terms of making adjustments in surgical strategies for older patients.

High BMI emerged as a significant predictive factor for overall complications (28.4%) after gastrectomy in older gastric cancer patients in the present study. The greater overall morbidity among the overwieght and obese patients resulted primarily from the high incidence of wound infections, corresponding to almost 27.5% of the patients with complications. Despite the surgical complexity caused by excessive subcutaneous fat, patients with high BMI are more likely to exhibit insulin resistance and poor glycemic control, both of which have been confirmed as risk factors for slow wound recovery.19-21 The metabolic states of high BMI patients may also alter the volume of distribution and clearance of drugs, thus impairing the effectiveness of standard antibiotic agents, which may also contribute to the relationship between high BMI and wound infection.22 The high incidence of wound infections and overall complication rates have been confirmed by the majority of previous reports.23-25 Consistent with the results of the present research, various studies have also shown that obesity affects the occurrence of postoperative complications due to cardiac complications and pulmonary embolism, in addition to wound infections.26-30 Although no anastomotic leak was present in any of the patients in this study, previous authors have reported that massive abdominal adipose tissue may result in a thick mesenterium and increased anastomotic tension.31

Nutrition assessment tools that incorporate inflammatory factors, such as the PNI and CONUT scores, have been developed to predict the postoperative morbidity and mortality of various cancers following radical surgeries.12-14 PNI and CONUT scores are attractive tools since both are based on mathematical equations, can be measured from single blood collections, are judged objectively, and can be safely applied in the clinical setting. The PNI and the CONUT score have both been assessed as predictors of perioperative morbidity for gastric cancer.32-35 A higher overall incidence of clinically significant postoperative complications

has been observed in patients with low PNI and high CONUT scores. In the present study, although these were significantly correlated with the occurrence of overall complications at univariate analysis, neither was significantly correlated at multivariate analysis.

Limitations

This study has several limitations. In particular, it involved the experience of a single center, and the sample size was limited. The study was also non-randomized, and we only analyzed prioritized potential predictive factors, based on their simplicity, objectivity, and preoperative availability, for overall complications after curative gastrectomy in patients aged 65 or over.

CONCLUSION

The overall postoperative complication risk was significantly higher in patients with high BMI among older individuals with gastric cancer who underwent curative gastrectomy. Older patients with high BMI were more likely to experience wound infections, cardiac and vascular complications. Perioperative management with a focus on BMI is important in older patients undergoing elective curative gastrectomy.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Samsun University Medical Faculty Clinical Researches Ethics Committee (Date: 21.10.2021, Decision No: GOKA/2021/21/10).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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